IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	LaVallie et al.		
Application No.:	08/949,904	Group Art No.:	1642
Filed:	October 15, 1997	Examiner:	Ungar
For:	Human SDF-5 Protein and Composition		
Confirmation No.:	8744		
Customer No.:	22204		

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Declaration Under 37 C.F.R. §1.132

Sir:

I, Edward R. LaVallie, declare the following in support of the above-identified application.

I am a Ph.D. candidate in the Department of Pharmacology at Boston University School of Medicine, nearly completed with the dissertation research. I hold an M.S. from the University of Connecticut in Microbiology. I also hold a B.S. in Biology from American International College.

I currently serve as a Senior Scientist /Associate Director at Wyeth where I work on research and development on osteoarthritis, muscular dystrophy, atherosclerosis, obesity, and asthma in the Department of Discovery Medicine. I have previously worked on hematopoeisis and the bacterial expression of mammalian proteins. I have worked continuously in the biotechnology and pharmaceutical industries for over twenty-one years.

I have included an updated copy of my *curriculum vitae* (Exhibit A) documenting my educational and professional background, along with a list of publications, patents, and presentations on which I have contributed as an author.

By virtue of my research, I am very knowledgeable regarding the current literature, theory, and recent developments relating to *in vitro* and *in vivo* models.

I am familiar with U.S. Patents, and I am named as an inventor on many pending patent applications and on thirty-seven (37) issued U.S. patents.

I am submitting this Declaration on behalf of the Assignee of the instant application in order to declare that the *in vitro* data in Example 7 of the specification (pgs. 52-53) represents an acceptable *in vitro* model that is expected to reasonably correlate with *in vivo* results. The *in vitro* data is derived from the MLB13MYC-clone 14 cell line, as described in Rosen, V., et

al. (*Journal of Bone and Mineral Research*, 9(11): 1759-1768 (1994)) hereinafter "Rosen" (Exhibit B).

I am familiar with the prosecution history of this patent application, having read in particular the specification, the currently pending claims, and the Examiner's position regarding *in vitro* data, as set forth in the Office Action dated November 12, 2003 (Exhibit C).

In order to analyze the disclosed *in vitro* utility, I reviewed Rosen in light of my own knowledge of the state of the art relating to cell lines and *in vivo* activity. Specifically, I reviewed the specification and Rosen in order to determine if the activity of the cell line should reasonably correlate with *in vivo* activity.

The Examiner alleges that with regard to "the *in vitro*, cell culture assay, for the reasons of record, no one of skill in the art would believe that the invention could be used as suggested based only on the cell culture information provided in the specification" (Exhibit C, p. 3, lines 10-13).

Rosen asserts that the response of these cells to growth factors (BMP-2 in the specific example in the paper) is likely to recapitulate the *in vivo* condition; Figure 5 depicts a model of *in vivo* differentiation that the authors propose, based upon their observations with the MLB13MYC-clone 14 cells. Therefore, the authors believe (and we concur) that the *in vitro* responsiveness of these cells can reasonably mimic the *in vivo* condition; in fact, it is the very premise of the paper. The final paragraph in the Rosen paper reiterates this premise.

The increase in cartilage markers in Example 7 demonstrates that SDF-5, in combination with BMP-2, is involved in the regulatory pathway for the formation of cartilage. The present invention, as set forth in the claims, can therefore be used in the treatment of cartilage disorders, such as osteoarthritis, rheumatoid arthritis, and articular cartilage defects. The use of SDF-5 in combination with BMP-2 to increase cartilage formation is a credible utility.

As one of skill in the art, I believe that the *in vitro* data as set forth in the instant patent specification reasonably supports applications *in vivo*. Accordingly, I disagree with the Examiner's assessment set forth in the Office Action dated November 12, 2003, and, in particular, to the statements alleged therein.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that

these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application or any patent issuing thereon.

Edward R. LaVallie
Senior Scientist
Associate Director
Wyeth Research

NOTARY

Commonwealth of Massachusetts }
ss:
Middlesex }

On the 30th day of March 2004, Dr. Edward R. LaVallie personally appeared before me, known by me to be the same person described in and who executed the foregoing instrument, and acknowledged that he executed the same, of his own free will and for the purposes set forth.

Paula M. Gaete, Notary Public
Commonwealth of Massachusetts
My Commission Expires 10/31/2008